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12 **UNITED STATES DISTRICT COURT**
 13 **FOR THE SOUTHERN DISTRICT OF CALIFORNIA**
 14

ILLUMINA, INC. and ILLUMINA)	Case No. 3:12-cv-01465-BEN-BGS
CAMBRIDGE LTD.,)	
)	DEFENDANT COMPLETE
Plaintiffs,)	GENOMICS, INC.'S RESPONSIVE
)	CLAIM CONSTRUCTION BRIEF
v.)	
)	Date: July 18, 2013
COMPLETE GENOMICS, INC.,)	Time: 9:00 A.M.
)	Judge: Hon. Roger T. Benitez
Defendant.)	Place: 5A
)	

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CITATION CONVENTIONS

The following citation conventions are used in this brief:

- CGI = Complete Genomics, Inc.
- Illumina = Illumina, Inc.
- '930 patent = U.S. Patent No. 8,192,930
- XX:YY = column number:line number(s) of referenced patent
- Ex. = Exhibit
- All Exhibits refer to the exhibits attached to the Declaration Of Marisa Williams In Support Of Defendant Complete Genomics, Inc.'s Opening Claim Construction Brief (Dkt. No. 45-1)
- Emphasis added unless noted as part of the original
- Internal citations have been omitted
- OB = citations to Illumina's Opening Claim Construction Brief, filed May 29, 2013 (Dkt. No. 44)
- '597 patent = U.S. Patent No. 6,306,597
- MPEP = Manual of Patent Examining Procedure
- Labbe Decl. = Declaration of John R. Labbe In Support Of Illumina's Opening Claim Construction Brief, filed May 29, 2013 (Dkt. No. 44-1)

I. INTRODUCTION

Because CGI's constructions are rooted in the specification, particularly sections such as the Summary of the Invention, which describe the invention as a whole, they should be adopted. Illumina's constructions are not only confusing and vague, but directly contradicted by the disclosures in the specification.

II. ARGUMENT

A. "in the same target double stranded polynucleotide"

1. **The Invention As A Whole, Not Just A Preferred Embodiment, Requires Attachment At The 5' Ends.**

The patent repeatedly states that attachment of both strands of the target double stranded polynucleotide is required by the *invention*:

- ***According to the invention*** . . . method comprising . . . *solid support having immobilised thereon* a plurality of double stranded template polynucleotides each formed from *complementary first and second template strands linked to the solid support at their 5' ends*. 3:32-40 (Summary of the Invention).
- ***The starting point for the method of the invention*** is the provision of a plurality of template polynucleotide duplexes *immobilised on a solid support* in the form of amplified clusters . . . The duplexes are each formed from *complementary first and second template strands which are linked to the solid support at or near to their 5' ends*. 5:59-6:1.
- The amplification of single molecules of such ditags to produce a clustered array *wherein both strands of each amplified duplex are immobilised, as taught for the first time by the present inventors*, confers a significant advantage in that it is possible to simultaneously analyse a large number of ditags of different sequences *on a single solid support*. 10:54-60.
- *See also* 20:52-60 (describing a "key feature of the invention"); 6:21-25; 26:55-60; 3:4-9, 64-65; 26:47-51; 4:9-12, 22-24; 8:58-59; 9:42-44; 13:26-27.

Accordingly, attachment is not merely a preferred embodiment, as Illumina argues, but rather is a critical "starting point" central to the whole invention. *See* 5:59-6:1.

a. **The Repeated Statements That The Invention Requires Both Strands Attached At The 5' Ends Limit Claim Scope.**

The Federal Circuit teaches that when a patent "describes the features of the 'present invention' as a whole, this description limits the scope of the invention."

1 *Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1308 (Fed. Cir.
 2 2007); *Edwards Lifesciences LLC v. Cook Inc.*, 582 F.3d 1322, 1329-30 (Fed. Cir.
 3 2009) (description of “intraluminal devices” as “the present invention” or “this
 4 invention” indicated an intent to limit “graft” to intraluminal devices); *Honeywell*
 5 *Int’l, Inc. v. ITT Indus., Inc.*, 452 F.3d 1312, 1318 (Fed. Cir. 2006) (four references
 6 to fuel filter as “the present invention” or “this invention” limited the scope of the
 7 claim term “fuel injection system component” because “the public is entitled to take
 8 the patentee at his word and the word was that the invention is a fuel filter.”). The
 9 ‘930 patent did not, as Illumina argues, merely “anticipate” that the invention *could*
 10 *be used* with attachment; rather, it identified attachment of both strands at the 5’
 11 ends as “the starting point for the method of the invention.” 5:59-6:1.

12 Thus, statements about the entire invention limit claim scope, not merely
 13 negative “disclaimers” as Illumina suggests. For this reason, the case law cited by
 14 Illumina is distinguishable. In *Enzo Biochem, Inc. v. Applera Corp.*, 599 F.3d
 15 1325, 1333 (Fed. Cir. 2010), the decision to not read “hybridization” into the claim
 16 rested largely on the absence of a suggestion in the specification that hybridization
 17 should be read into the claim. In *Northrop Grumman Corp. v. Intel Corp.*, 325 F.3d
 18 1346, 1355 (Fed. Cir. 2003), the patent never indicated “that the invention can be
 19 used only with a ‘command/response’ protocol” and did not limit the claim. By
 20 contrast, the ‘930 patent instructs that “[a]ccording to the invention,” the method
 21 begins with a double-stranded polynucleotide attached at the 5’ ends. 3:32-40.

22 **b. Illumina Fails To Show That Attachment Is Not Required.**

23 This conclusion is further bolstered by Illumina’s failure to identify a single
 24 example in the patent where attachment is not used. The sole passage Illumina
 25 insists contemplates alternatives to attachment (OB at 16-17) actually supports
 26 CGI, as it confirms that attachment to a solid support is “required” for sequencing:

27 In certain embodiments of the invention covalent attachment may be
 28 preferred, but *generally all that is required is that the molecules (e.g. nucleic
 acids) remain immobilised or attached to the support* under the conditions in

1 which it is intended to use the support, for example in applications requiring
2 nucleic acid amplification and/or sequencing.

3 6:19-25. Illumina also argues that attachment at the 5' ends is not required. But
4 Illumina points to no disclosure of attachment other than at the 5' ends. Illumina
5 points only to a separate patent—mentioned once in passing in a different context—
6 to show disclosure of attachment at the 3' ends of the strands. OB at 17. In itself,
7 this illustrates that the '930 patent does *not* disclose 3' attachment. Moreover, as
8 explained in Section II.B.2, this is not sufficient to broaden the claim scope.

9 **2. Claim Differentiation Does Not Apply.**

10 First, as a threshold matter, claim differentiation only applies when there is
11 complete redundancy between claims. *Kraft Foods, Inc. v. Int'l Trading Co.*, 203
12 F.3d 1362, 1368 (Fed. Cir. 2000) (“only . . . at least one limitation must differ.”).
13 Here, however, the claims each add further limitations: Claim 2 adds, at least,
14 monitoring of the sequencing reactions and labeled nucleotides; Claims 3-8 add, at
15 least, primer hybridization by heating and cooling or after chemical denaturation;
16 Claims 9-23 add, at least, an internal known primer region; and Claims 24-26 add,
17 at least, use of pluralities of template double-stranded polynucleotides on a
18 clustered array. As each claim differs in scope, claim differentiation is irrelevant.

19 Second, even if claim differentiation did apply (which it does not), it is flatly
20 rebutted by the specification. *Retractable Techs., Inc. v. Becton Dickinson and Co.*,
21 653 F.3d 1296, 1305 (Fed. Cir. 2011) (“claim differentiation ‘will be overcome by
22 a contrary construction dictated by the written description or prosecution history’”).
23 A recent Federal Circuit case is instructive. In *American Calcar v. American*
24 *Honda Motor Co.*, 651 F.3d 1318 (Fed. Cir. 2011), “messages” was construed to
25 require an address that uniquely identifies the vehicle to which the message is being
26 sent, and the format “<vehicle-id>@<domain>.” *Id.* at 1329. ACI invoked claim
27 differentiation, arguing that when the inventors intended to include an address in
28 the message, they did so by expressly reciting that requirement in a claim, as shown

in dependent claim 2. *Id.* at 1336. The Federal Circuit declined to apply claim differentiation because the specification indicated that the *entire* invention required messages to contain an address. *Id.* at 1337. The Summary of the Invention stated that a message has an address identifying the vehicle and the Detailed Description of the Invention stated that “in accordance with the invention,” the address must use the format “<vehicle-id>@<domain>.” *Id.* While dependent claim 2 is presumed to be narrower than independent claim 1, “claim differentiation is not a conclusive basis for construing claims, and the [] specification overrides its effect here.” *Id.* Similarly, here, claim differentiation, even if applicable, would be rebutted by the specification, namely, statements advising that attachment of both strands to solid support is the “starting point for the method of the invention.” 5:59-6:1. A narrow construction is “required to tether the claims to what the specification[] indicate[s] the inventor actually invented.” *Retractable*, 653 F.3d at 1305.

3. Viewed In The Proper Legal And Factual Context, The Prosecution History Does Not Support Illumina’s Arguments.

Illumina’s story about the prosecution history does not stand up. A claim is anticipated if “each and every element as set forth in the claim” is found in a single prior art reference. MPEP § 2131. “During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow.” *In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989). This differs from the mode of interpretation applied by a court in an infringement case, and usually interprets the claim to be broader than it is when construed according to the specification. *Id.* at 321-22.

Thus, in considering whether Claim 1 was anticipated, the Examiner looked at the *recited* elements of Claim 1, applied the *broadest possible interpretation*, and identified prior art that met each of those recited elements. Indeed, her rejection of Claim 1 over Weimann corresponded exactly to the recited elements of the claim:

Weimann teaches a method for pairwise sequencing of first and second regions of a double stranded polynucleotide wherein said first and second regions are in the same target double-stranded polynucleotide, the method

comprising hybridising and reading from a first primer, removing the first primer and hybridising and reading from a second primer at a different location in the same target double stranded polynucleotide.

Ex. O at 6. Attachment is not a *recited* element of Claim 1; therefore, the Examiner did not directly address it. Illumina’s own responses confirm as much. Illumina stated, for example, that the prior art failed to “disclose or suggest all of the *recited elements* of the claims” Ex. R at 11. Thus, when viewed in context, that O’Meara was not cited against Claim 1 does not compel the conclusion that attachment is not required.

This is especially true in view of the contrary evidence in the prosecution history. When Illumina added new Claim 1, it told the Examiner that the sole specific support for the addition of this claim was in Claim 2. Ex. N at 8. If Illumina had considered Claim 1 to dispose of the attachment requirement present in the other claims, it could not have cited only Claim 2 as its specific support—it would have had to identify where the specification teaches practicing the invention without attachment (but, as shown in Section II.A.1., no such disclosures exist).

Even if the prosecution history helped Illumina, “when the prosecution history appears in conflict with the specification, any ambiguity must be resolved in favor of the specification.” *Lydall Thermal/Acoustical, Inc. v. Federal-Mogul Corp.*, 344 Fed. App’x 607, 614 (Fed. Cir. 2009). Indeed, “[r]epresentations during prosecution cannot enlarge the content of the specification.” *Id.*; *Honeywell*, 452 F.3d at 1318-19 (finding no broader claim scope in prosecution as statements were “ambiguous and possibly inconsistent with the written description” and trumped by “clear statements in the specification”). Thus, the specification’s advisement that attachment is the first step of the method “[a]ccording to the invention” trumps the muddled argument Illumina contrives from the prosecution history. 3:32-40.

Finally, *Morvil Tech., LLC v. Medtronic Ablation Fronteirs, LLC*, No. 10-cv-2088, 2012 WL 3277272 (S.D. Cal. Aug. 10, 2012) is distinguishable. First, this

1 Court cited several reasons for choosing the plaintiff's construction, most notably
 2 that it found support in the specification and the defendant's proposed construction
 3 would exclude a preferred embodiment. *Id.* at *4-5. The prosecution history was
 4 another data point consistent with the rest of the evidence. Second, the Court stated
 5 that the prosecution history only "suggests" that the plaintiff's construction was
 6 correct; it was not treated as dispositive. *Id.* at *5. Here, the prosecution history
 7 not only fails to suggest a conclusion, but is directly belied by the specification.

8 **4. Illumina's Construction Is Overly Broad And Unclear.**

9 Illumina's construction, not CGI's, would confuse the jury. The term
 10 "original polynucleotide duplex" in Illumina's construction is vague and could
 11 capture sequencing methods that have preceded, and fall outside the scope of, the
 12 patent. For example, "original polynucleotide duplex" could signify the following:
 13 the DNA double-helix that exists in every living cell; the double-stranded DNA
 14 extracted from cells for laboratory use (or naturally single-stranded RNA converted
 15 into double-stranded DNA); or the double-stranded polynucleotide that is actually
 16 attached to solid support and sequenced. But only this last option, which comports
 17 with CGI's construction, is touted as the invention's "starting point." 5:59-6:1.

18 **B. "reading from a [first/second] primer"**

19 **1. The Invention As A Whole, Not Just A Preferred Embodiment, 20 Requires The Successive Incorporation Of Nucleotides.**

21 The patent repeatedly states that successive incorporation of nucleotides into
 22 a polynucleotide chain is a characteristic of the *invention*, thus limiting claim scope:

- 23 • ***According to the invention*** . . . the method comprising . . . performing a
 24 [first/second] sequencing reaction by *sequential addition of nucleotides* to the
 25 [first/second] sequencing primer to generate a [first/second] extended
 26 sequencing primer 3:32-51, 56-63 (Summary of the Invention).
- 27 • The ***method of the invention*** is described in further detail as follows . . .
 28 sequencing reaction proceeds via *successive incorporation of nucleotides* to
 the [first/second] sequencing primer. 20:20-21; 21:13-18, 24-31.

- 1 • Sequencing can be carried out using *any suitable “sequencing-by-synthesis”*
2 *technique*, wherein *nucleotides are added successively . . . , resulting in*
3 *synthesis of a polynucleotide chain in the 5' to 3' direction.* 21:32-36.
- 4 • The ***methods of the invention*** are not limited to use of the sequencing
5 method outlined above, but can be used in conjunction with essentially any
6 sequencing methodology *which relies on successive incorporation of*
7 *nucleotides into a polynucleotide chain.* 22:9-13.

8 **2. Illumina Wrongly Attempts To Import Into The '930 Patent The**
9 **Disclosures Of The Entire '597 Patent.**

10 The '597 patent was litigated in *Illumina, Inc. and Solexa, Inc. v. Complete*
11 *Genomics, Inc.*, No. 10-cv-05542 (N.D. Cal.), Illumina's first lawsuit against CGI,
12 and found to be invalid and not infringed. Illumina now attempts to re-litigate this
13 patent, contending that a single reference to the '597 patent at Column 22 somehow
14 pulls in the '597 patent's every disclosure and claim, dramatically expanding the
15 scope of the '930 patent to include sequencing methods never otherwise discussed.

16 **a. The '597 Patent Is Mentioned Only Once In The Entire**
17 **Patent And Is Not Even Incorporated By Reference.**

18 The '597 patent is mentioned in passing once in the forty columns of the '930
19 patent and is not incorporated by reference. 22:17. Illumina knew how to
20 incorporate references into the patent, and had done so with multiple references.
21 *See, e.g.*, 5:59-63 (“whose contents are *incorporated herein by reference*”); 10:7;
22 22:39-42; 27:1-3; 1:11-15. But Illumina chose not to use such “incorporation by
23 reference” language in its sole mention of the '597 patent. This “mere reference” to
24 the '597 patent does not incorporate it into the patent. *See* 37 C.F.R. § 1.57(b)(1) &
25 (g)(1) (incorporation by reference must use “the root words ‘incorporat(e)’ and
26 ‘reference’ (e.g., ‘incorporate by reference’))” (“A *mere reference* to material does
27 not convey an intent to incorporate the material by reference.”); *Application of De*
28 *Seversky*, 474 F.2d 671, 674 (C.C.P.A. 1973) (“mere reference” was insufficient).

Even if the '597 patent was “incorporated by reference,” it does not have the
effect Illumina urges, because Illumina did not “identify with detailed particularity

1 what specific material it incorporates and clearly indicate where that material is
 2 found.” *See Adv. Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed.
 3 Cir. 2000); *see also SkinMedica, Inc. v. Histogen Inc.*, No. 09-cv-122, 2011 WL
 4 2066619, at *6-7 (S.D. Cal. May 24, 2011) (same). Incorporation by reference
 5 “does not convert the invention of the incorporated patent into the invention of the
 6 host patent.” *Modine Mfg. Co. v. USITC*, 75 F.3d 1545, 1553 (Fed. Cir. 1996)
 7 (abrogated on other grounds).

8 **b. Even If The ‘597 Patent Was Incorporated By Reference, It**
 9 **Would Not Support Illumina’s Overly Broad Construction.**

10 Illumina’s assertion that the ‘930 patent now covers all methods of
 11 sequencing by ligation is belied by the specification, particularly the very paragraph
 12 in which the ‘597 patent is mentioned. The entire paragraph reads as follows:

13 The methods of the invention are not limited to use of the sequencing method
 14 outlined above, but *can be used in conjunction with essentially any*
 15 *sequencing methodology which relies on successive incorporation of*
 16 *nucleotides into a polynucleotide chain*. Suitable techniques include, for
 17 example, Pyrosequencing™, FISSEQ (fluorescent in situ sequencing), MPSS
 18 (massively parallel signature sequencing) and sequencing by ligation-based
 19 methods, for example as described in U.S. Pat. No. 6,306,597.

20 22:9-17. This preceding sentence is inherently limiting. To the extent the patent’s
 21 method can be used with another sequencing methodology, it is limited to uses
 22 relying on the *successive incorporation of nucleotides into a polynucleotide chain*.
 23 Thus, there is only one possibly consistent reading of the ‘597 patent in view of the
 24 ‘930 specification, and it supports CGI’s construction. The ‘597 patent, though
 25 primarily directed to sequencing by ligation with oligonucleotides, also teaches the
 26 incorporation of *nucleotides* using polymerase. *See, e.g., Labbe Decl., Exh. B, Fig.*
 27 *4, 9:47-56, 11:15-38, 14:54-63*. This interpretation comports with the disclaimer
 28 that the invention can be used with techniques that rely on the incorporation of
 nucleotides. Indeed, the reference to “sequencing by ligation-based methods”
 implies that techniques *based on* other sequencing methods could be combined with

1 the patent as long as they also teach successive incorporation of nucleotides into a
2 polynucleotide chain. Illumina's construction would read out this disclaimer.

3 Incorporating any more of the '597 patent would contradict the teachings in
4 the rest of the specification, which describe sequencing as the successive
5 incorporation of *nucleotides*. See *Smartphone Techs. LLC v. Research in Motion*
6 *Corp.*, No. 6:10-cv-74, 2012 WL 489112, at *4 (E.D. Tex. Feb. 13, 2012) (rejecting
7 attempt to read an embodiment from an incorporated reference into the claims
8 because it was contradicted by the definition in the specification). Indeed, the '930
9 patent does not teach sequencing by ligation anywhere in the patent. It does not
10 teach sequencing with ligase. It does not teach sequencing with oligonucleotides.
11 Nor does it teach sequencing in the 3' to 5' direction (in any event, ligase can also
12 sequence in the 5' to 3' direction, consistent with CGI's construction). It explicitly
13 limits itself to sequencing that relies on the *successive incorporation of nucleotides*.

14 Finally, Illumina never explains how the paragraph at Column 22 actually
15 supports its construction. Even assuming that the '597 patent was incorporated by
16 reference (which it was not), Illumina must make a sizeable leap to argue that
17 "reading" means "obtaining sequence information" with no regard to the particular
18 sequencing method used. Illumina never bridges this disconnect. It likewise never
19 explains why the explicit outer boundary set on the sequencing methods used with
20 the invention (*i.e.*, "any sequencing methodology which relies on successive
21 incorporation of nucleotides into a polynucleotide chain") can be ignored. In sum,
22 Illumina cannot dramatically expand the scope of the invention based on an isolated
23 statement that lacks support in, and is even contradicted by, the specification.

24 **3. The Other Elements Of CGI's Proposal Are Rooted In The Patent.**

25 First, while Illumina points out that CGI's proposed language "determination
26 of the nature of the nucleotide after each incorporation" refers to a "particular
27 embodiment," it is the broadest embodiment disclosed in the patent. Claim 1, the
28 only independent claim, appropriately captures the broadest disclosed embodiment.

Every other means of identification described in the patent is a narrower subset of, and thus covered by, CGI's construction (*e.g.*, labeled nucleotides, fluorescence, etc. (21:36-22:8)). Illumina points to no embodiment that is not covered by CGI's construction. Second, while Illumina argues that the bases in each read need not be contiguous, it ignores that the bases must be read "*from* a [first/second] primer." Merely reading "near" a primer does not comport with the patent.

C. "removing the first primer"

First, CGI's construction is taken from the specification passage teaching removing the first primer according to the "method of the invention" (20:20-21):

When the first sequencing reaction is complete, the extended first sequencing primer is removed from the surface. This can be achieved by heating, or chemical denaturation.

21:24-26. CGI is faithful to the specification by incorporating each element above into its construction. Illumina never contests the accuracy of this construction. *See* OB at 23 ("Illumina agrees that 'removing' can include 'heating and chemically denaturing'") ("Illumina agrees that in the context of the entire claim, the step of 'removing the first primer' follows the step of 'hybridizing and reading from a first primer'"). Nor does Illumina identify any element that is excluded from CGI's construction—Illumina does not point to any part of the patent in which removal is accomplished by a means other than heat or chemical denaturation, from a place other than the surface, or at a time other than after the first sequencing reaction.

Second, "removing the first primer"¹ is far from a "commonly-understood" term that requires no construction. Unlike in *Netflix*, where a juror could "understand through everyday experience" the meanings of the words "movie" and

¹ Illumina argues that "removing" is a commonly-understood word, but the term is "removing the first primer," which is not commonly-understood. *Cf. Gen-Probe Inc. v. Becton Dickinson and Co.*, No. 09-cv-2319, 2011 WL 7167137, at *17 (S.D. Cal. Nov. 22, 2011) ("penetrated by," "penetrated," and "penetrating" referenced penetrating a seal, which a juror could understand from experience).

“item” in the context of a movie rental queue, the average juror has no experience with removing a primer. *See* OB at 22; *Netflix, Inc. v. Blockbuster, Inc.*, 477 F. Supp. 2d 1063, 1068 (N.D. Cal. 2007). Because this term warrants construction, and Illumina offers no proposal, CGI’s construction should be adopted.

D. “first and second regions”

First, CGI adopts, verbatim, the specification’s definition of this claim term: The *first and second regions* for sequence determination are either on the same strand, or on complementary strands, of the double-stranded polynucleotide template 5:54-57. The construction that most naturally aligns with the description of the invention and stays true to the claim language “will be, in the end, the correct construction.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005). Illumina objects to construing this term in the very way the specification defines it and never explains why this definition should be ignored. Second, CGI’s proposal reflects that the regions are distinct, not necessarily separate. The Summary of the Invention describes only “distinct” regions. Illumina acknowledges that “distinct” is repeated throughout the specification. OB at 11.

E. “different location”

As shown above, CGI’s construction accurately reflects that the regions are found at distinct locations. CGI’s construction is appropriately tied to the regions for sequence determination. The purpose of the patent is to sequence two regions in the target double-stranded polynucleotide. 3:23-26. CGI’s construction signifies that the regions are distinct locations in the target double-stranded polynucleotide.

III. CONCLUSION

For these reasons, CGI’s constructions should be adopted.

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1 Dated: June 12, 2013

Respectfully submitted,

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3
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6 Attorneys for Defendant
7 COMPLETE GENOMICS, INC.
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PROOF OF SERVICE

I am an attorney, and on June 12, 2013, I caused a true and correct copy of
DEFENDANT COMPLETE GENOMICS, INC.'S RESPONSIVE
CLAIM CONSTRUCTION BRIEF

to be served by electronic service via the Court's CM/ECF system. In accordance
 with the electronic filing procedure of this Court, service has been effected on the
 parties below, whose counsel are registered participants of CM/ECF, via electronic
 service through the CM/ECF system:

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I declare under penalty of perjury that the foregoing is true and correct.
 Executed this 12th day of June, 2013.

/s/ Marisa Armanino Williams
 Marisa Armanino Williams